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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,526	WILKINSON ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-48 is/are pending in the application.

4a) Of the above claim(s) 8,9,13,15-18,20,22-25,31 and 33-38 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7,10-12,14,19,21,26-30,32 and 39-48 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the following species A-D:

A. Plurality of random polynucleotide segments selected from: random segments from at least two distinct gene regulatory elements as recited in claim 7; B. A selection step as recited in claim 12 as currently amended; C. A segment formation as recited in original claim 19, preferably in claim 19 as currently amended in more generic form to also incorporate claim 21, and D. Progenitor polynucleotides as recited in claim 32 as currently amended, and that it consists of more than one transcriptional regulatory elements as recited in claim 39.

Applicants state that claims 1-7, 10-12, 14, 16, 19, 21, 26-30, 32, 39-48 are readable on the elected species. Accordingly, claims 8-9, 13, 15-18, 20, 22-25, 31, 33-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Status of Claims

Claims 1-48 are pending

Claims 8-9, 13, 15-18, 20, 22-25, 31, 33-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species.

Claims 1-7, 10-12, 14, 19, 21, 26-30, 32 and 39-48 are under examination.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claims 19 and 21 reciting cleavage by the broad "mechanical" cleavage. Claim 28 "wherein the nucleotides sequence of the oligonucleotides are not from a transcriptional regulatory polynucleotide." Claim 47 "wherein the assembling step does not comprise a polymerase".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10-12, 14, 19, 21, 26-30, 32 and 39-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A). To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention.

Applicants at the time of filing do not have possession of the claimed genus. The disclosure describes only specific species that does not correlate to the huge scope of the genus claim. It describes a method as specifically adapted for the promoter assembly of a specific progenitor for the two plant species, the strawberry vein-banding virus 35S-like ((SVBV) of Seq. ID. 1 Example 9) Brassica napin promoter. It also describes Aspergillus alcohol dehydrogenase promoter, its mutants and a spike compound thereof. It does not describe a method for the

claimed progenitor genus from which segments can randomly be obtained and reassembled. There is no correlation made for the specific species to the huge scope of the claimed progenitor from which different segments can be randomly obtained and reassembled. It fails to indicate the kind of polynucleotide comprising the progenitor gene. The location, kind and/or length of the segments that can be derived from said progenitor gene. Neither does the number of genes that comprised a random polynucleotide is described nor the kind of assay or means by which a randomly reassembled polynucleotide, especially from a heterologous polynucleotide is made. The disclosure of specific species within a genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicants have invented species sufficient to constitute the gen[us]. Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004). The evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). To satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e.,

structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus.

The claimed method encompasses a huge scope of polynucleotide sequence or segment of homologous or heterologous promoter from different species derived from the huge scope of progenitor polynucleotide. The three species would not be considered a representative of the huge scope of the genus claim. Normally, the identity and location of cis-acting regulatory elements within a promoter are generally not known. It is not apparent whether recombination of random DNA segments within a promoter combined with a defined activity.

The specification further provides only a list of progenitor polynucleotides; cell and tissue -specific promoters of plants. However, a listing of every possible progenitor polynucleotide does not constitute a written description of every species in a genus. It would not reasonably lead those skilled in the art to any particular species. In re Ruschig, 379

F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967). In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. This is evident from Li et al (US 2002/0168640) disclosure at page 8, [0107]. Li states ".. it is important to understand that in any library system encoded by oligonucleotide synthesis one cannot have complete control over the codons that will eventually be incorporated into the peptide structure. This is especially true in the case of codons encoding stop signs…" Due to the high level of DNA binding specificity of transcription factors, each transcription factor will typically bind to a different DNA sequence. In some instances, a related family of transcription factors may bind to the same DNA sequence. Selection of the sequences used in the hybridization probes may be based on the different tfs that one wishes to detect in a sample. This in turn may depend on the type of organism, cell, or disease state one wished to identify and/or monitor the gene expression of. It is noted that different organisms will also express different activated transcription factors and the expression level could be biased. Thus, applicants, at the time of filing are not in possession of the huge scope of the genus of the progenitor polynucleotide

that results in a random segment from a homologus or heterologous polynucleotide. The numerous factors or variables included in the genus are infinite. One may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claim unless the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples.
A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

B). Claims 1-7, 10-12, 14, 19-21, 26-30, 32 and 39-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining which progenitor polynucleotide or fragments, either a homologous or heterologous progenitor can be combined to produce a random library. That is, a library of transcriptional regulatory polynucleotide with a different transcriptional regulatory activity than the progenitor polynucleotide (homologous or heterologous in kind). It does not describe the location, the number of fragments that can be derived from each of the progenitor polynucleotide or all the possible combinations to form a plurality of random segments for reassembly.

2). The specification failed to provide working examples for the numerous and/or different types of progenitor

polynucleotide containing different transcriptional regulatory polynucleotide of homologous kind, let alone of the heterologous type.

3). The breadth of the claims encompasses a large diversity of random segments of transcriptional regulatory polynucleotide from a homologous or heterologous progenitor to form a reassembled polynucleotide. It is well known in the art that the diversity of the inserts in a vector or host is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert, especially for biological methods.

4). The state of the prior art is such that techniques or methods are specifically applied or adapted for a known progenitor polypeptide from which a random transcriptional regulatory segments can be derived.

5). The art is inherently unpredictable because it is not possible to predict that even with a predetermined progenitor polynucleotide, the fragments that can be randomly combined with other fragments to reliably predict an expression library in which each of the reassembly polynucleotide are equally

expressed. It is generally known in the art that there are still no rules that have emerged that allow even for a defined polynucleotide structure of a progenitor to be related to sequence in any simple fashion (even as applied to the actual compounds).

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art to the numerous undefined variables of the claimed method e.g., progenitor polynucleotide, the random transcriptional regulatory segments from the progenitor polynucleotide and other unpredictable factors. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 7, 10, 12, 14, 19, 21, 26, 29, 39-41 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Chuzhanova et al (Gene).

Chuzhanova et al disclose at page 10 under Materials and methods section up to page 17 a method of identifying a reassembled polynucleotide comprising obtaining from a plurality of gene promoters of growth hormone (GH1, GH2 and GH) from vertebrate species and human prolactin gene promoter. The technique termed complexity analysis was used to obtain fragments from the gene promoters of GH. Fragments from single and pair wise decompositions that occurred for at least two GH gene promoter sequences or sequence pairs were included in a vocabulary of blocks (i.e., assembly of the plurality of segments in a random fashion, as claimed) and merging into a single block the fragments (reassembly of the plurality as claimed) and identifying the reassembled polynucleotide as shown in Table 2. The specific method steps of Chuzhanova using specific gene regulatory components fully meet the broad claimed method.

Claims 1, 5, 7, 10, 12, 32 and 39-41 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Punnonen et al (Science and Medicine).

Punnonen et al discloses at pages 38-41 a method of DNA shuffling of e.g., antigens where any DNA sequence can be subjected to DNA shuffling and screening. It comprises obtaining a starting material (progenitor as claimed) from a family of homologous sequence obtained from natural diversity, a single gene or a set of synthetic DNA sequences. The starting gene of two or more homologous genes is randomly fragmented by DNAse digestion. The random-length DNA fragments are subsequently reassembled into full-length sequences by polymerase reaction. Fragments derived from the different parent sequences act as both primers and templates. A fragment from one sequence can hybridize with a fragment from another creating chimeras that have shuffled components between family members. The genomes (page 39, col. 1) can be of animals, plants and microbes and can be used as the starting material (progenitor, as claimed). Punnonen discloses at page 46, a library of promoters with a broad range of activities created by the method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

> the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 10-12, 14, 19, 21, 26-30, 32 and 39-41 and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chuzhanova et al or Punnonen et al in view of Ni et al (The Plant Journal) or Short (6,238,884).

Punnonen is discussed above. Punnonen does not describe the reassembled polynucleotide comprises an enhancer (claim 11) or that the oligonucleotide sequence corresponds to a transcription binding site. However, Ni disclose at page 661, col. 2 that most eukaryotic promoters contain enhancer elements, that by binding trans-acting factors define the promoter strength and tissue specific expression pattern. Short discloses at col. 51, line 59 up to col. 52, that eukaryotic DNA transcription can be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting sequences of between 10 to 300 bp that increase transcription by a promoter. Enhancers are effective if located within an intron or within the coding sequence itself. It would have been obvious to one having ordinary skill in the art at the time the invention was used to use enhancers in the method of either Chuzhanova or Punnonen as taught by Ni or Short. The advantages taught either by Ni or Short would

provide the motivation to one having ordinary skill in the art to use enhancers.

Claims 43-47 are obvious over the disclosure of Short at e.g., col. 30,line 29 up to col. 31, line 15; col. 57, line 45-64.

Claims 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chuzhanova et al or Punnonen et al in view of Cui et al (The Plant Journal) as applied to claims 1-7, 10-12, 14, 19, 21, 26-30, 32 and 39-41 and 48 above, and further in view of applicants' disclosure of known prior art.

Each of Chuzhanova and Punnonen is discussed above. Each of these references does not disclose the limitation as recited in claims 42-47. However, applicants state at paragraph [36], that genomic DNA or CDNA comprising nucleic acids of the invention can be identified in standard Southern blots under stringent conditions using the nucleic acid sequences. Suitable stringent conditions for such hybridizations are those which include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37OC, and at least one wash in 0.2X SSC at a temperature of at least about 500C or equivalent conditions. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar

stringency. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the stringent conditions (Southern blots) in the method of Chuzhanova or Punnonen as such conditions is conventional using the known Southern blot stringent hybridization, as recognized by applicants above. Said washing condition is a result-effective variable well within the ordinary skill in the art to determine, at the time of filing.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
June 13, 2005